

junior, was encouraged, provided he could substantiate what he said. Rigid scientific standards had to be maintained and proper evidence provided. 'Opinion' was at once, fairly politely, denounced. A quiet humour added savour to over-turgid discussion and Dr McMichael had a constant care for comprehensibility so that no point was missed. ('What exactly do you mean by "C.V.A."? Ah yes, I thought you were talking about the coronary vessels: some people use it to mean "Cerebro-Vascular Accident": we might as well all mean the same thing.') And he was invariably punctiliously polite to the patient who was being demonstrated, taking care to put him at his ease.

Dr McMichael was not actually made Professor until Sir Francis Fraser became Director

of the British Postgraduate Medical Federation and resigned from the Chair. It made little difference. Professor McMichael had been Professor in all except name for years. Nor did the honours which crowded on him—Membership of the Medical Research Council, a term on the Medical team of the University Grants Committee, Fellowship of the Royal Society, a richly deserved Knighthood, Wellcome Trusteeship. All these left him still the same modest, competent teacher and Director of the Department of Medicine, a very wonderful man. His leaving the School might have been a disaster, but in fact it provided an association, through the Federation, instead of what would otherwise have been an imminent retirement. Long may he be spared to radiate a new and benign influence from Guilford Street.

## Oliver and Schäfer's discovery of the cardiovascular action of suprarenal extract

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MANY of us have heard a story of the discovery of adrenaline. Oliver is supposed to have applied an instrument for measuring the internal diameter of the radial artery to his young son. Having given his son an injection of an extract of the suprarenal gland, Oliver thought that he detected a change in the diameter of the artery. He then went to London to Schäfer and found him engaged in an experiment in which the blood pressure of the dog was being recorded. When Schäfer's experiment was finished Oliver persuaded him to inject some of his suprarenal extract into a vein. They then stood amazed to see the mercury mounting in the arterial monometer till the recording float was lifted almost out of the distal limb. This episode has been recounted by Dale (1938, 1948) and is based on a strong tradition, surviving in the Department of Physiology at University College, when Dale was there from 1902 to 1904 (personal communication).

According to T. R. Elliot (1934) Oliver 'had devised apparatus to measure the calibre of the peripheral arteries in man, and he had observed that when doses of a glycerin extract of supra-

renal glands were given by the mouth to his son they made him sick and caused constriction of the radial artery. A superficial observer would have passed by this, and satisfied himself with an explanation from the supposed toxic action of the extract. Oliver would not do so. Half an explanation is worse than none, for it may lead to contented disregard of the new truth that lies beyond. Oliver sought the test of a laboratory experiment and went to Schäfer at University College. That was in 1893, when hormones and glands as such were unknown to physiology. Oliver took his extract with him and Schäfer consented to inject some of it into the vein of a cat upon which he had just finished some other blood pressure experiment. The writing point of the record ran sharply up the drum and Schäfer was suddenly introduced to a new field of physiology, the action of the endocrine glands.'

Oliver and Schäfer's demonstration to the Physiological Society of 'The physiological action of extract of the suprarenal capsules', was given at the meeting of 10 March 1894 at University College (Oliver & Schäfer, 1894).

Figure 1 is a photograph of the staff of the

department at that time. Schäfer, Jodrell Professor, is the central figure. Standing above and to the left, in the grey overcoat, is Oliver (Fig. 1).

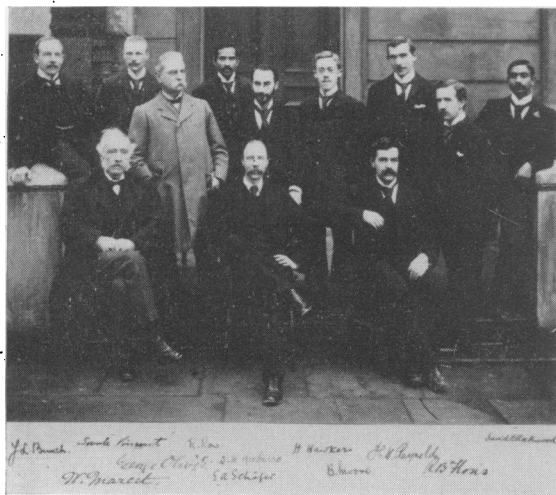


FIG. 1

George Oliver (1841–1915) had one son Charles (1873–1940) and one daughter Madge (1874–1924). If Oliver administered an extract of suprarenal capsules to his young son then it would have been into Charles, who was aged about 20 in 1893. Charles Oliver was an engineer, an inventor, and the founder of what is now Oliver-Bell Control Ltd, Woolwich. Charles Oliver's nearest living relatives are his only son, Mr G. F. Norris Oliver, Managing Director of Oliver-Bell Control Ltd, his only daughter Miss Ruth Oliver and his first cousin Lady Sander-son. None of these recalls having heard of Charles Oliver as having been the subject of an investigation by his father; nor does Miss Geraldine Sharpey-Schafer, daughter of E. A. Schäfer and friend of Charles Oliver's sister Madge Oliver.

Both Oliver and Schäfer say that Oliver administered the extract by the mouth and not by injection.

Oliver (1895a) says: 'During the winter of 1893–4, while prosecuting an inquiry as to the agents that vary the calibre of the arteries as determined by an instrument (the arteriometer) which I have elsewhere described, I found that the administration by the mouth of a glycerine extract of the adrenals of the sheep and calf produced a marked constrictive action on the arteries.... This position has since been confirmed by a research undertaken by Professor Schäfer and myself in the Physiological Labora-

tory of University College.' And again, 'Having observed that the radial calibre is reduced by suprarenal extract (m xv. = gr. xv. of suprarenal capsule by the mouth). I was led to determine whether the contraction of the arteries resulted from injection of the extract into the veins of the animals; and Professor Schäfer and myself are now engaged in an experimental enquiry "On the Physiological Effects of Suprarenal Extract" in which we have conclusively proved this fact.' (Oliver 1895b).

Schäfer (1908) says, 'In the autumn of 1893 there called upon me in my laboratory at University College a gentleman who was personally unknown to me, but with whom I had a common bond of interest—seeing that we had both been pupils of Sharpey, whose chair at that time I had the honour to occupy. I found that my visitor was Dr George Oliver, already distinguished not only as a specialist in his particular branch of medical practice, but also for his clinical application of physiological methods. Dr Oliver was desirous of discussing with me the results which he had been obtaining from the exhibition by the mouth of extracts of certain animal tissues, and the effects which these had in his hands produced, upon the blood vessels of man, as investigated by two instruments which he had devised—one of them the haemodynamometer, intended to read variations in blood pressure, and the other, the arteriometer, for measuring with exactness the lumen of the radial or any other superficial artery. Dr Oliver ascertained, or believed he had ascertained, by the use of these instruments, that glycerine extracts of some organs produce decrease in calibre of the arteries and increase of pulse tension, of others the reverse effect.

Although the conclusions were interesting, it was easy to see that results which were obtained under mechanical conditions, which were somewhat complex and not easy of interpretation, could not be expected to decide an important physiological question of this nature, and that it was essential, in order to obtain exact knowledge of the actions, if any, of such extracts, to conduct the investigations with the employment of all means at the disposal of the modern physiologist. With the suggestion that we should undertake such an investigation Dr Oliver promptly agreed, and it was then and there arranged to devote that winter to a thorough examination of the physiological effects of such extracts. The result of this conjunction of effort, brought about by the fortunate chance foreseen by old Montesquieu, speedily showed that, whilst many of the extracts which had been dealt with

clinically by Oliver were inert or at any rate not specific in their action, the suprarenal capsules, and to a lesser extent the pituitary body, yielded to glycerine and to water and to saline solutions principles which have an extraordinary effect upon the tone of the heart and arteries, transcending that of any known drug. . . .

In 1895, Oliver addressing the Section of Pharmacology and Therapeutics of the Annual Meeting of the B.M.A. spoke at some length about the clinical administration of extract of the suprarenal capsules (Oliver, 1895a): 'In the earlier part of this enquiry I employed a tincture and a dried aqueous extract; but I now prefer tablets of the dried gland (gr. iii, and v in each), which are equal to about five times their weight of the dried gland. I have always found it best to maintain the effect of administration of a tablet at regular intervals—for example, twice or three times a day within an hour after meals. I have given the adrenal preparation for lengthened periods without observing any injurious effect; for instance a patient has taken the tincture (m xv = gr. xv of the fresh gland) three times a day for just 12 months. Moreover in one case of diabetes, I did not observe any distressing effect from eight gr. v tablets (each equivalent to grs. xv of the fresh gland) taken three times a day for a week. But this is the only case in which I have given comparatively large doses. I have always preferred to feel my way, guided mainly by a sense of wellbeing in the patient, and the readings of the arteriometer; and whenever I have observed signs of undue arterial tension and of oppression, or a marked degree of infrequency of the pulse (as in one case a reduction to 54) I have either diminished the dose or given it less frequently. In the majority of cases a 3-grain tablet three times, or after a time twice a day, or a 5-grain tablet twice a day, has sufficed to maintain a favourable effect. . . . Some years later Oliver (1901) considered rectal administration as preferable to oral, but

only for a short time. In the first Oliver-Sharpey Lecture Oliver (1904) presents results he obtained in man following the administration of 1½ hemisin tabloids, Burroughs Wellcome and Co. (= 0.00045 gramme adrenaline). Discussing these results he says: 'Should we not take the hint and prescribe only in such small doses as a half a hemisin tabloid in the tumbler of water with meals.'

Space does not permit discussion of other aspects of Oliver's work. Such questions as 'Why did Oliver begin his work on the effects of organ extracts,' 'Of what organs did he make extracts,' 'Did Oliver's suprarenal extract really cause constriction of the radial artery,' and if so, 'Why,' since adrenaline given by the mouth is generally supposed to be ineffective, such questions are outside the scope of this paper, the aim of which is only to point out that, according to Oliver and to Schäfer, Oliver administered his extracts by the mouth.

#### Acknowledgments

We gratefully acknowledge help from Mr Norris Oliver, Miss Ruth Oliver, Lady Sanderson, Miss Geraldine Sharpey-Schafer and Miss Gillian McKenzie.

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